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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,891	11/17/2000	Susan R. Webb	TSRI 536.1Div2	7205

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The Scripps Research Institute
10550 North Torrey Pines Road
Mail Drop TPC-8
La Jolla, CA 92037

EXAMINER

VANDERVEGT, FRANCOIS P

ART UNIT PAPER NUMBER

1644

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/715,891

Applicant(s)

WEBB ET AL.

Examiner

F. Pierre VanderVegt

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61-82 and 149-164 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 61-71, 73, 75, 77-82, 149-152 and 157-160 is/are rejected.
- 7) ☒ Claim(s) 72, 74, 76, 153-156 and 161-164 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

DETAILED ACTION

This application is a divisional of U.S. Application Serial Number 09/194,285, which is a rule 371 continuation of application serial number PCT/US97/08697, which claims priority to provisional application 60/018,175.

Applicant should amend the priority data on page 1 of the specification in order to display the relationship to the PCT application, as the provisional application lapsed prior to the filing of the '285 application.

Claims 1-60 and 83-148 have been canceled.

New claims 149-164 have been added.

Claims 61-82 and 149-164 are currently pending in this application and are the subject of examination in the present Office Action.

1. In view of Applicants response filed May 10, 2004, only the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 61-71, 73, 75, 77-82, 149-152 and 157-160 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for accessory molecules selected from the costimulatory molecules B7.1 and B7.2, the adhesion molecules ICAM-1, ICAM-2, ICAM-3 and LFA-3 and the survival molecules Fas ligand and CD70, does not reasonably provide enablement for other types of accessory molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It was previously stated: "The claims are most broadly drawn to the construction of a "poikilothermic synthetic antigen presenting cell" (APC) comprising an intact Class II MHC molecule and an "accessory molecule." The instant specification discloses the accessory molecules B7.1, B7.2 (costimulatory molecules), ICAM-1, ICAM-2, ICAM-3, LFA-3 (adhesion molecules), Fas ligand and CD70 survival molecules). Beyond the disclosed elements, the term "accessory molecule" encompasses any molecule which may participate in the processes of antigen processing and/or presentation, including

Art Unit: 1644

all molecules which have a role from capture and uptake of an antigenic molecule by an APC to internal molecules which chaperone the antigen or break up larger proteins into epitope peptides, molecules which assist the association of the epitope with the Class II molecule and cytokines which stimulate the activation of reactive T cells, as all such molecules perform accessory functions to MHC class II. The specification does not teach molecules which participate in all aspects of antigen processing and presentation and therefore does not provide sufficient guidance to one of ordinary skill in the art to practice the claimed invention commensurate in scope with the recitation of "accessory molecules."

In view of the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute."

As a first note to clarify the record, by the use of "any and all" in the statement of rejection as previously presented, it was the Examiner's intent to indicate accessory molecules "other" than those enumerated in the statement and not include those enumerated.

Applicant's arguments filed May 10, 2004 have been fully considered but they are not persuasive. Applicant asserts that the full scope of the invention is enabled because the specification has exemplified eight different accessory molecules and because the specification "teaches" generic accessory molecules. This argument is not convincing, however. First of all, a "teaching" of generic accessory molecules does not provide any information regarding the functionality of any of those generic molecules, nor does it provide any structural information to the artisan about the structural features of the generic molecules or how those generic molecules interact with the APC/T cell interaction or with the antigen processing pathway. Exemplifying eight accessory molecules provides information only about those eight molecules and is not reasonably predictive of the artisan's success in incorporating other types of accessory molecules into the claimed artificial APCs.

3. Claims 61-71, 73, 75, 77-82, 149-152 and 157-160 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was previously stated: "The written description in this case only sets forth insect cells that have been transformed to express MHC class II heterodimers and accessory molecules. The term "poikilothermic synthetic antigen presenting cell" in the claims broadly encompasses any type of cell derived from an organism having a body temperature that varies with the temperature of its surroundings, including such ectotherms as fish or reptiles. Applicant has not disclosed other cell types that would be suitable for use in making the claimed synthetic APCs, only stating that insect cells are particularly well suited for use (page 8, lines 4-13 for example). The instant specification does not describe other cell types, nor are vectors suitable for the transformation of non-insect cell types described.

Art Unit: 1644

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that “Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See *Vas-Cath* at page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

Accordingly, the written description in this case only sets forth insect cells as the source cell lacking any one of the components of the MHC class II heterodimer or an accessory molecule for the manufacture of synthetic APCs.”

Applicant argues that the written description requirement has been met because the specification “sets forth, for example, eukaryotic poikilothermic cells that have been transformed to express MHC class II heterodimers and accessory molecules (see, e.g., page 8, lines 4-31 of the specification).” However, the cited passage recites only that “[i]t is preferable to use a poikilotherm cell line because MHC molecules are thermolabile. A range of species are useful for this purpose...Eukaryotic cells and preferably insect cells are used as APC. Preferred insect cells include Drosophila (fruit fly) and Spodoptera (butterfly). MHC class II molecules have been expressed in insect cells such as Drosophila and Spodoptera cells.” Accordingly, the specification sets forth only Drosophila and Spodoptera cells, representative of insect cells, as “eukaryotic poikilothermic cells that have been transformed to express MHC class II heterodimers and accessory molecules,” stating only the use of poikilothermic cells in general is a preferred embodiment. The specification does not set forth any information relevant to other poikilotherms, such as fish or reptiles. The specification does not disclose any other type of poikilothermic cell or vectors or promoters suitable therefore. Applicant counters by citing the recitation of a number of different eukaryotic vectors usable in the claimed invention. However, it is noted that

4. Claims 61-71, 73, 75, 77-82, 149-152 and 157-160 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using synthetic MHC class II positive antigen presenting cells via transfection of insect cells, does not reasonably provide enablement for utilizing cells from other poikilothermic organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It was previously stated: “Briefly, the claims are most broadly drawn to the making and using of a “eukaryotic poikilothermic synthetic antigen presenting cell” (APC) which can present antigen in the context of MHC class II. The claim therefore reads upon any cell that is derived from an organism having a body temperature that varies with the temperature of its surroundings. The breadth of the claim therefore encompasses cells from ectothermic animal sources as diverse as reptiles, fish, echinoderms, mollusks and nematodes, for example. The instant specification exemplifies cells and vectors

Art Unit: 1644

representative of insect species, more specifically, *Drosophila melanogaster*. The instant specification provides guidance by which the artisan can transfect insect cells with the MHC subunits and the accessory molecules and express said molecules on the surface of the insect cell. However, the specification is not enabling for the transfection and use of other types of cells. There is no disclosure of vectors which are suitable for transfection of other cell types, nor is there a disclosure of culture conditions, such as media supplements required, for the propagation and maintenance of non-insect poikilothermic cells. It would require an undue amount of experimentation on the part of the artisan to devise expression vectors and establish culture conditions for cells from other types of organisms, such as echinoderms, which would be conducive for the expression of MHC class II heterodimers and requisite accessory molecules on the cell surface for that cell to effectively function as an effective APC.

In view of the nature of the invention, quantity of experimentation necessary, the limited working examples, the state and unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute."

Applicant has traversed this ground of rejection on the grounds that the specification sets forth eukaryotic poikilothermic cells in general and that the culture conditions for poikilothermic cells in general is known in the art. However, as stated supra, vectors used in *Drosophila* were modified by Applicant to comprise *Drosophila*-specific sequences for incorporation into the genome of the target cells (page 36 for example) and that the transformation of *Spodoptera* cells was carried out using *Spodoptera*-specific vectors (page 35 for example). There is no such species-specific teaching for any other poikilotherm. Enablement reaches beyond the knowledge of culture conditions by the artisan. The artisan must also possess or be provided with the knowledge of species-specific vectors or of required modifications to eukaryotic vectors required for expression in a given poikilothermic species. Therefore, absent a showing that expressing foreign gene products in a variety of poikilothermic was well known to the artisan at the time the invention was made, such knowledge must be imparted by the instant specification and this is clearly not the case.

Conclusion

5. Claims 72, 74, 76, 153-156 and 161-164 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH**

Art Unit: 1644

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
August 9, 2004

PV

Pat J. Nolan
PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
8/9/04